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JOURNAL OF ETHNOPHARMACOLOGY
An interdisciplinary journal devoted to bioscientific research
on indigenous drugs

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OPE

Early man, confronted with illness and disease, discovered a wealth of useful therapeutic agents the plant and animal kingdom. The empirical knowledge of these medicinal and toxic substances s passed on by oral tradition, and was eventually annotated in herbals and *materia medica*.

Many valuable drugs of today (*e.g.* atropine, digitalis, reserpine) have come into use through a idy of folk remedies, and many plant natural products have served as prototypes of synthetic drugs.

Complementing the achievements of modern medicine, the scientific search for new drugs from isting indigenous healing preparations continues. Reports of anthropological and ethnobotanical ld studies and the results of research carried out with modern analytical techniques employed by ytochemists and pharmacognosists fall within the journal's scope.

The *Journal of Ethnopharmacology* will publish research papers concerned with the observation, scription and experimental investigation of the biological activities and the active substances of plants d animals used in the traditional medicine of past and present cultures. The journal will particularly elcome interdisciplinary papers with an ethnopharmacological, an ethnobotanical or a chemical apoach to the study of indigenous drugs.

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Articles in this journal will be indexed and abstracted in Chemical Abstracts, Current Advances Plant Science, Current Anthropology, Current Contents, Excerpta Botanica Section A: Taxonomica Chorologica, Excerpta Medica, Index Medicus, International Pharmaceutical Abstracts, Medicinal d Aromatic Plants Abstracts, Psychopharmacology Abstracts, and Science Citation Index.

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Review Paper

MEDICINAL PLANTS IN TROPICAL WEST AFRICA
I. PLANTS ACTING ON THE CARDIOVASCULAR SYSTEM

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(Received May 6, 1980; revised form accepted July 15, 1980)

General introduction

This paper is the first of a series of review articles to be assembled later in one volume, to be published as a sequel to the monograph on *Medicinal Plants in Africa* which I wrote in 1960. This latter was a critical survey of the scattered information available about drug plants found in Nigeria; it suggested a first choice of the plant material which seemed potentially more important, and made suggestions concerning points requiring further scientific investigation (constituents, pharmacology, *etc.*).

As medical science develops and becomes more organized in the West African countries, the time would seem to have come to re-assemble and update our knowledge of the subject and extend it to the whole of Tropical West Africa. Furthermore, greater importance is now being attached to the use of locally available medicines as a means of reducing reliance on expensive imported drugs.

Since the first book appeared, a number of papers have been published dealing with the chemical analysis, pharmacology and clinical action of West African plants. The new book will cover the whole of Tropical West Africa, not just Nigeria. Supplementary information now available about individual plants will be included and the range of plants considered will be more extensive.

This time, I shall attempt to classify the drugs according to their established or possible medical uses, this being the best way of rapidly assessing the medical interest of any particular drug. The value of the drug will depend on several factors:

(A) whether it is the only drug, or one of the few drugs, used in the treatment of a disease;
(B) whether the disease in the treatment of which it is used is a common one;
(C) whether it is less toxic than other existing drugs for a particular purpose;

Group B. Plants containing cardiotonic alkaloids

Erythrophleum guineense G. Don CAESALPINIACEAE
Ordeal tree, sasswood, red water tree, sassy bark

L. The bark has been used in arrow poisons; its toxic aqueous decoction or cold infusion is called "red water" and was used in fetish trials and ordeals*. Rigal (1941) observed that in guinea pigs death occurred after 3 hours with a dose of 0.5 g/kg and after 55 minutes with 1 g/kg. The seeds were found to be more toxic than the bark in spite of a lower alkaloid content. Probably this is due to the simultaneous presence of a strongly haemolytic saponin (Rigal, 1941). In local medicine the bark is sometimes used as a diuretic, emetic and sternutatory.

C. Bark and seeds contain 0.1 - 0.5% of total alkaloids, mainly erythrophleine (Paris and Rigal, 1940, 1941), also cassaine, cassaidine, norcassaidine, coumingine, and erythrophleguine (Dalma, 1939; Lindwall *et al.*, 1965). Apart from the alkaloids, a catechuic tannin, a saponin and a flavonoside (luteolin glycoside) have been isolated from the bark, as well as a wax with a high proportion of hexacosanol. Erythrophleum ivorense Chev. = *E. micranthum* Harms. is less toxic than *E. guineense* probably because of a higher tannin and a lower alkaloid content (up to 0.3%).

The cardioactive properties of the alkaloids can be destroyed by saponification and can be changed by chemical modifications. Thus, modification on C-3 of cassenic acid produces a stronger and longer lasting action (Hauth, 1971).

P. Erythrophleine has a digitalis-like action, whilst the action of coumingine, which is the most active, is similar to that of scillaren A in the cat. Cassaine and cassaidine are less potent than erythrophleine which raises the blood pressure, slows the pulse while increasing the force of the heart beat and decreases respiration (Cotten *et al.*, 1952). Overdoses produce symptoms of circulatory depression, breathing difficulties, vomiting and, through direct action on the medulla, convulsions. Erythrophleine is said to be of use in spasmodic asthma (Rigal, 1941). It also has a local anaesthetic action similar to cocaine but more powerful and longer lasting. However, no use has been made so far of this action, probably because of the general toxic effect of the alkaloids (Trabucchi, 1937). Derivatives of the alkaloids are being prepared in an attempt to decrease their toxicity (Hauth, 1971). In low concentrations cassaine and coumingine increase the translocation of K^+ from the plasma to the cells (Kerharo, 1968).

A bark extract of Erythrophleum sauveolus (Guill. & Perr.) Brenam has been shown to have strong spasmogenic effect on smooth muscles. It also has a chronotropic and isotropic effect on the heart and shows a potent hypotensive action probably mediated through release of catecholamines (Bamgbose, 1974).

Voacanga africana Stapf = *V. glabra* Schum. = *V. Schweinfurtii* var. *parviflora* Schum. = *V. magnifolia* Wernham = *V. talbotti* Wernham = *V. eketensis* Wernham = *V. glaberrima* Wernham = *V. africana* var. *glabra* (Schum.) Pich.
APOCYNACEAE

Locally the latex is used as a rubber adulterant and is applied to carious teeth (Oliver, 1960).

Since 1955 this plant has aroused considerable interest and has been the subject of numerous publications. From the bark of the stem and the root many alkaloids have been isolated (4 - 5% in the stembark and 5 - 10% in the rootbark). These include voacamine (the main alkaloid), voacangine, voacristine (= voacangarine), voacorine, vobasine, voacamidine (isomer of voaca-

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*In trials by ordeal (e.g. trial of Lander in Badagry in 1827) a man suspected of evil influence or action was forced with much ceremony to swallow a dose of poison. If he considered innocent. If he died this mine) and many others. Most of these alkaloids have also been found in *V. thouarsi* Roem. & Schult. and some in other species of *Voacanga*, *Tabernaemontana* and even *Alstonia*. In the leaves of *V. africana* voaphylline and vobtusine are found, tabersonine in the seeds (Blanpin *et al.*, 1961; Puisieux *et al.*, 1965; Oliver-Bever, 1967).

Voacamine and voacangine act on the heart in a similar way to the cardiac glycosides but their toxicity is very low in comparison with that of other alkaloids with a cardiostimulant action, such as the *Erythrophleum* alkaloids. One hundred micrograms of voacamine sulphate have a cardiotonic action equivalent to 0.25 units of digitalis standard (in isolated rabbit auricles) (Oliver-Bever, 1967). It does not bind itself to the cardiac proteins and has no cumulative action, but it has a direct myotonic effect on the cardiac fibre (Quevauviller and Blanpin, 1957a). Lethal doses for guinea pigs (by instillation in the jugular vein) are 313 mg/kg for voacamine sulphate and 348 mg/kg for voacangine sulphate, compared to 2.5 mg/kg for digitalin and 0.9 mg/kg for strophanthin. In mice the LD_{50} of voacangine is 41 - 42 mg/kg intravenously (La Barre and Gillo, 1955; Vogel and Uebel, 1961). Therapeutic doses (1 - 3 mg daily) are well tolerated, act rapidly and are quickly eliminated without any cumulative effect. Voacamine, voacangine and voacorine also have a hypotensive action and are simultaneously mildly parasympatholytic and sympatholytic. Voacangine, which is also said to have an analgesic and a local anaesthetic action, and vobtusine increase the hypnotic effect of barbiturates. Voacorine is also cardiotonic through direct action on the heart muscle and on the coronary perfusion and seems to contribute considerably to the action of the total alkaloids of *Voacanga* (Quevauviller and Blanpin, 1957b). Its minimum LD_{50} in guinea pigs (by slow intravenous injection) is 288 mg/kg (Blanpin *et al.*, 1961).

For the leaf alkaloid vobtusine the LD_{50} is 33.75 mg/kg intravenously. It has a depressive action on the heart and has hypotensive and sedative properties (Quevauviller *et al.*, 1965). Tabersonine from the seeds has a hypotensive action equivalent to 25% that of reserpine (Zetler, 1964).

II. Cardiac depressants — anti-arrhythmic agents

Argemone mexicana L. (naturalised) PAPAVERACEAE
Mexican poppy, prickly pepper, prickly poppy

The plant is used in Nigeria and Senegal mainly for its diuretic, sedative, cholagogic and cicatrizing properties (Oliver, 1960; Kerharo and Adam, 1974). The seeds have a cannabis-like effect and the herb, juice and flowers are reputed to be narcotic in many countries (Watt, 1967).

Numerous alkaloids have been reported in all parts of the plant. Thus, leaves, stems and seeds contain berberine and protopine and the roots coptisine, α-allocryptopine, chelerythrine and dihydrochelerythrine. In the oil of the seeds sanguinarine and dihydrosanguinarine are found (Chakravarti *et al.*, 1954; Bose *et al.*, 1963). Argemonine was isolated from leaves and capsules and identified as *N*-methylpavine (Martell *et al.*, 1963).

α-Allocryptopine (0.099%), found in the roots of the plant in Czechoslovakia, is identical to α-fagarine. It slows down the heart rate and prolongs systole in rats and frogs. In doses of 10 - 20 mg/kg it also slows down the heart beat of cats and rabbits. The action is a direct one on the myocardium and is also antifibrillatory, and α-allocryptopine has found clinical applications in this field. Thus it is considered more active than quinidine in cases of arrhythmias with fibrillation and auricular flutter (Alles, 1952; Dhar *et al.*, 1968; Manske and Holmes, vol. 5, pp. 90 - 91).

Protopine was isolated from the total alkaloid fraction by Bose. He reported that it stimulated the heart, blood pressure and respiration, as well as the striated and smooth muscles on which it appears to act specifically (Manske and Holmes, vol. 5, pp. 92 and 138).

The seed oil is highly toxic due to sanguinarine (the LD_{50} for mice is 1.8 mg per 100 g subcutaneously). Sanguinarine can produce experimental glaucomas (Hakim, 1954).

Berberine is relatively non-toxic (the LD_{50} in cats and dogs is 0.025 mg per 100 g intravenously). In doses of 2 mg/kg, berberine has a depressant and vasodilating action on the heart. It also depresses breathing but stimulates the smooth muscles of different organs (intestine, uterus, bronchi). Moreover, berberine has marked antibiotic properties on *Mycobacterium tuberculosis*, *Staphylococcus aureus*, *Escherichia coli*, *Eberth typhosa* and *Shigella dysenteriae*, and it also acts on *Leishmania tropica* (Lambin and Bernard, 1953) at concentrations of 1:80000. An alcohol–water extract of the fruits deprived of the seeds proved to be an excellent hypnotic and sedative for convulsions and spasmodic conditions (Martínez, 1959, p. 110). Antifibrillatory action has also been reported in oleandrin from *Nerium oleander* described earlier under cardiotonics (Fauconnet and Pouly, 1962).

Fagara zanthoxyloides Lam. = *F. senegalensis* (D.C.) Chev. = *Zanthoxylum senegalense* D.C. = *Z. polygamum* Schum. RUTACEAE
Prickly ash, candlewood, toothache bark

The aromatic rootbark is used in Ghana and Nigeria as a decoction, or in application, for its alleged antiseptic and analgesic properties, for example in the treatment of painful conditions, childbirth, toothache, *etc.*, sometimes mixed with other ingredients. The decoction is also used as a vermifuge and in Guinea the bark is used to stupefy fish. The fixed oil contained in the rootbark causes salivation, a numbing action on the tongue and paralysing effects (Pobeguin, 1912; Irvine, 1930; Dalziel, 1937; Oliver, 1960).

An amorphous alkaloid was isolated from the root as early as 1887 and called artarine. [Later this was found to be identical with ethoxychelerythrine (Torto *et al.*, 1969).] Then in 1911 a pungent principle which produced salivation was extracted from the rootbark. It was called fagaramide, and proved to be an *N*-isobutylamide of piperonylacrylic acid.

Since 1947 a number of tertiary and quaternary alkaloids have been identified in the bark and rootbark of *F. zanthoxyloides*. These were, in addition to artarine, β-fagarine (= skimmianine, a dimethoxydictamnine),

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CHUCHUHUASHA — A DRUG USED IN FOLK MEDICINE IN THE AMAZONIAN AND ANDEAN AREAS. A CHEMICAL STUDY OF *MAYTENUS LAEVIS*

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Summary

In the high Amazonian basin a plant named *chuchuasha*, (or *chuchuaso*) is used in traditional medicine for several purposes in the form of an alcoholic extract. This plant, a *Maytenus* species, most probably *Maytenus laevis*, grows in the subandean region of the Amazonian basin (Peru, Ecuador, Colombia).

Antitumor and anti-inflammatory properties were recently attributed to the extracts of the root bark of the plant. The composition of the extract of *M. laevis* from the Putumayo area of Colombia was studied in order to establish the active principle responsible for these activities. The presence of phenoldienones (tingenone, 22-hydroxytingenone), a catechin (4′-methyl-(—)-epigallocatechin) and proanthocyanidins (Ouratea-proanthocyanidins A and B) was established.

The biological activities of these compounds confirm the properties of the extracts of the plant claimed by traditional medicine.

In several areas of the subandean rain forest in the Amazonian river basin, mainly in Peru, Ecuador and Colombia, a plant known as *chuchuhuasha* or *chuchuhaso* is used by several tribes: Pastazas, Ticunas, Boras, Huitotos, Pebas, Yahuas, Cocamas, Aguarunas and Jívaros. The powdered red root bark is used as an alcoholic infusion, generally in *aguardiente*, as a general tonic, for the treatment of rheumatism and even as an aphrodisiac. For topical use it is employed as an antitumoral agent in skin cancer and also for the treatment of sores.

A large ethnobotanical literature has flourished on *chuchuhuasha* and many different plants have received this name, giving rise to a certain confusion. It is usually agreed (Colas, 1937) that the plants used belong to the genus *Maytenus* (Celastraceae). This is in accordance with the name *curi-caspi*, which means "golden bark", given by the Jívaros to the plant. In fact, some